## REMARKS

### I. The rejection under 35 U.S.C. § 112, second paragraph, should be withdrawn.

The Examiner rejected claims 9-13, 41 and 45-47 as assertedly being indefinite because the metes and bounds of what would constitute the "size" of unprocessed VEGF-D in the sample allegedly cannot be determined. Applicants disagree.

First, it should be noted that that the Examiner prompted the inclusion of the step of determining the size of VEGF-D recited in claim 45. In the previous Office Action, the Examiner asserted that, "In order to detect unprocessed versus processed VEGF-D, the size of VEGF-D in the sample must be determined." (Office action mailed May 2, 2007 at page 2.) Because the Examiner indicated that a step comprising determining the size of VEGF-D was required to be in the claims, it appears that current rejection would have to have been considered by the Examiner before issuing the previous Office Action. Therefore, Applicants introduction of new claim 45 did not necessitate this new ground of rejection.

Claim 45 specifically recites determining both the amount and the size of the VEGF-D in the sample. The specification provides various teachings for determining the amount and size of VEGF-D in a sample. For example, by subjecting a sample to electrophoresis or other size separation techniques, histochemistry can be used both to quantify and to measure the size the protein of interest. To provide just one example technique, a Western blot is useful for assessing both size and quantity of a protein of interest, such as VEGF-D. The present application discloses the use of such a technique to assess the size of VEGF-D. See, for example, Example 9 (and, in particular, paragraph [0148]) and Example 13. The size of unprocessed VEGF-D (~53 kd) as well as the sizes of the various other forms of VEGF-D are identified in paragraph [0113] and in Figure 2 of the present application. Thus, one of ordinary skill in the art would understand the metes and bounds of the size of unprocessed VEGF-D.

The Examiner further asserts that claim 45 is allegedly incomplete for missing the step of contacting the sample with an antibody that binds to unprocessed VEGF-D. To the contrary, the claim is complete as drafted because it recites a step of measuring the

amount and size of VEGF-D and the specification discloses how to measure the amount and size of VEGF-D in a sample. Accordingly, one of skill in the art would appreciate upon review of the specification how to measure the amount and size of VEGF-D in the sample as recited in claim 45. Accordingly, claim 45 is indeed complete. Moreover, contacting the sample with an antibody that binds unprocessed VEGF-D is one variation described in the application, but it is not the only way for a person of ordinary skill to measure the amount and size of VEGF-D. (For example, the VEGF-D could be purified and then measured using conventional protein sizing and quantification techniques, or a different affinity reagent , such as a VEGF-D receptor peptide, could be used.)

In view of the foregoing, Applicants respectfully request that the rejections under 35 U.S.C. § 112, second paragraph, be withdrawn.

## II. The rejection under 35 U.S.C. § 102(b) should be withdrawn.

The Examiner rejected claims 9-13, 41 and 45-47 under 35 U.S.C. § 102(b) as allegedly being anticipated by WO 98/33485 ("Achen II"). Applicants request reconsideration of the rejection in view of the following remarks.

First, Applicants point out that Achen II was not cited as a reference under 35 U.S.C. § 102(b) in the previous Office Action. Rather, Achen II was considered by the Examiner in the previous Office Action for a rejection under 35 U.S.C. § 103(a). Applicants respectfully submit that the Examiner, while considering Achen II as a reference under 35 U.S.C. 103 would also have had to consider the reference under 35 U.S.C. § 102. Therefore, the present rejection could have been presented in the previous Office Action and was not necessitated by Applicants amendments to the claims. The present Office Action should not have been made final.

The present application discloses that increased amounts of ***unprocessed*** (i.e., full-length) VEGF-D expressed in tumors leads to faster tumor growth and increased metastatic risk than expression other forms of VEGF-D in tumors (i.e., fully processed or truncated portions of VEGF-D). See, Examples 9 and 13 of the present application.

The Examiner asserts that Achen II anticipates the pending claims because it discloses a method for diagnosing a neoplastic disease such as human malignant melanoma as an indicator of future metastatic risk. The Examiner points to page 20, lines 1-10, of Achen II in support of the rejection. Even if Achen II generically discloses methods of detecting VEGF-D in a sample and methods of screening for cancer associated with VEGF-D, Achen II does not specifically disclose or suggest measuring both the amount and **size** of the VEGF-D in the sample for ***diagnosing the growth characteristics*** of a neoplastic disease based on the amount of ***unprocessed*** VEGF-D in a sample. In fact, Achen II at page 20, line 10 states "**Quantitation** of VEGF-D in cancer biopsy specimens will be useful as an indicator of future metastatic risk" (emphasis added). Thus, Achen II teaches the amount of VEGF-D in the sample, and not the size of the VEGF-D, is useful as an indicator of metastatic risk.

Moreover, Achen II also does not specifically disclose that tumors expressing ***unprocessed*** VEGF-D generate more blood and lymphatic vessels than tumors expressing other forms of VEGF-D. The present application is the first disclosure of the association between the amount of ***unprocessed*** VEGF-D and the intensity of the resulting tumors.

The Examiner further asserts that the recitation measuring the size of VEGF-D in the sample is an inherent step because Achen II discloses an antibody (antibody "4A5") that binds to unprocessed VEGF-D. Applicants disagree with the Examiner's analysis. Achen II teaches that the 4A5 antibody was *generated against a processed form* of VEGF-D known as VEGF-DΔNΔC. (See Achen II at pp. 31-32.) Because antibody 4A5 binds to processed VEGF-D, the *in situ* experiments cited by the Examiner cannot be fairly interpreted as a measurement of the quantity of unprocessed VEGF-D. Analysis of a tissue section with an antibody that binds an epitope found in both unprocessed, partly processed, and mature VEGF-D can provide information about the distribution of VEGF-D in the sample and the total quantity of VEGF-D, but does not indicate which forms of VEGF-D are being measured. Thus, the Achen II experiments (which are repeated as Example 4 in the current application) do not teach "measuring the amount and size" of VEGF-D, and therefore Achen II does not anticipate the claims expressly or inherently.

Because Achen II does not specifically disclose methods of screening for a neoplastic disease characterized by an increase in the amount of ***unprocessed*** VEGF-D in cancers, it does not anticipate any of claims 9-13, 41 and 45-47. Anticipation requires that the cited art disclose each and every element of the claims, which is not the case here. In view of the foregoing, Applicants respectfully request that the rejection of claims 9-13, 41 and 45-47 under 35 U.S.C. § 102(b) be withdrawn.

## III. Conclusion

For the foregoing reasons, Applicants request withdrawal of all outstanding rejections and allowance of the pending claims. No other fees are believed to be due with the filing of this paper. However, the Director is authorized to charge any additional fees deemed necessary to Deposit Account No. 13-2855, under order number 28967/5680D.

If the Examiner believes that a telephone conversation would expedite allowance of the claims, she is invited to contact the undersigned agent or David A. Gass, attorney for applicants, at the number below.

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Respectfully submitted,

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